Examiner's Amendment and Comments

1. The Response and Amendment filed 22 July 2008 to Office Action mailed 17 April 2008 is acknowledged and entered.

Withdrawal of Rejection based on Applicant's Amendments

2. In view of remarks and amendments in the response filed 22 July 2008 to Office Action mailed 17 April 2008, the following rejections in Office Action mailed 17 April 2008 are hereby withdrawn:

- Anticipatory rejection to Claims 1-4, 6-9 and 16-18 under 35 U.S.C. §102(b) as anticipated by Cohn (U.S. Patent 4,868, 179) with evidence provided by Hunter et al (U.S. Patent 5,716,981 A).

- obviousness rejection to Claims 1- 4, 6-9, 12-13 and 16-25 under 35 U.S.C. § 103 (a) as obvious over combined teachings from Cohn (U.S. Patent 4,868, 179) in view of Hunter et al (U.S. Patent 5,716,981 A) and Klemsdal et al. ((1994. A New Isosorbide Dinitrate Extended-Release Formulation: Pharmacokinetic and Clinical Parameters in Patients with Stable Angina Pectoris. Eur. J. Clin. Pharmacol., 47:351-354) with evidence from Wikipedia (Anonymous, Isosorbide mononitrate. From Wikipedia Pages 1-4 Printed 10/18/2007) and further in view of Chobanian et al (U. S. Patent 5,645,839).

Claims Status

3. Claims 10-11, 14-15 and 26-169 are cancelled.

4. Claims 1-9, 12-13 and 16-25 are currently pending.

Examiner's Amendment

5. An Examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicants, an amendment may be filed as provided by 37 C.F.R. §1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this Examiner's amendment was given in a telephone interview on 01 August 2008 with Ms. Belinda M. Lew, Applicants' Representative.

In the Title:

Please change the current title with:

Composition for Treating Vascular Diseases Characterized by Nitric Oxide Insufficiency

In the Abstract

Please change the current Abstract with following Abstract:

The present invention provides a composition comprising an antioxidant, and at least one of isosorbide dinitrate and isosorbide mononitrate in therapeutically effective dosage of each of the aforementioned compounds to treat cardiovascular diseases caused by nitric oxide (NO) insufficiency. The antioxidant is a hydralazine compound.

In the Claims:

1. (Currently amended) A sustained release oral formulation comprising biodegradable microparticles and/or nanoparticles having dispersed therein a therapeutically effective amount of at least one antioxidant and at least one of the isosorbide dinitrate and isosorbide mononitrate, wherein the isosorbide dinitrate is present in an amount [[of]] to deliver about 30 milligrams per day to about 160 milligrams per day and/ or the isosorbide mononitrate is present in an amount to deliver about 5 milligrams per day to about 120 milligrams per day.

8. ((Currently amended) The sustained release oral formulation of claim 7, wherein the hydralazine hydrochloride is present in an amount [[of]] to deliver about 30 milligrams to about 400 milligrams per day.

9. ((Currently amended) The sustained release oral formulation of claim 8, wherein the hydralazine hydrochloride is present in an amount [[of]] to deliver about 50 milligrams to about 300 milligrams per day.

12 (Canceled)

13. (Currently amended) The sustained release oral formulation of claim [[12]] 1, wherein the isosorbide mononitrate is present in an amount [[of]] to deliver about 15 milligrams per day to about 100 milligrams per day.

18. (Currently amended) The sustained release oral formulation of claim 1, comprising ~~a therapeutically effective amount of~~ hydralazine hydrochloride as the antioxidant and isosorbide dinitrate.

19. (Currently amended) The sustained release oral formulation of claim 1, comprising ~~a therapeutically effective amount of~~ hydralazine hydrochloride as the antioxidant and isosorbide mononitrate.

Examiner's Reasons for Allowance

6. The closest art are:

- U.S. Patent 4,868, 179, issued 19 September 1989 to Cohn. Cohn teaches composition comprising hydralazine hydrochloride in a daily dose in range of 55 milligrams/day to 3, 000 mg/day and isosorbide dinitrate in a daily dosage of 30 milligrams/day to 160 milligrams/day; but said composition is not dispersed in a micro or nanoparticle;

- U.S. Patent 5,716,981 A issued 10 February 1998 to Hunter et al. Hunter et al., teach dispersal of pharmaceutical compositions in micro or nana materials but not comprising hydralazine hydrochloride and isosorbide dinitrate, especially to deliver daily dosages of each as claimed instantly;

- Klemsdal et al., published in Eur. J. Clin. Pharmacol., 47:351-354. Klemsdal et al. teach a either isosorbide dinitrate or isosorbide mononitrate to treat angina pectoris , but said composition does not comprise hydralazine hydrochloride; and

- U. S. Patent 5,645,839, issued 08 July 1997 to Hibernian et al. Hibernian et al. teach a composition comprising hydrolyzing acerbate and at least one pharmaceutically acceptable carrier, but not hydralazine hydrochloride, isosorbide mononitrate or dinitrate.

Thus, none of the cited references either separately or in combination teach a therapeutical composition dispersed in a micro-or mnanoparticle, wherein said composition comprises isosorbide dinitrate and/ or isosorbide mononitrate and hydralazine hydrochloride and additionally wherein said composition delivers the dosage for each one of isosorbide dinitrate and/ or isosorbide mononitrate and

hydralazine hydrochloride in daily dosages ranges instantly claimed. Accordingly, there is no motivation either intrinsic or explicit to combine the teachings from each one of the above-cited references to obtain instantly claimed invention.

7. Any comments considered necessary by applicants must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Examiner's Amendment and Comments."

8. Claims 1-9, 13 and 16-25 are allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Kailash C. Srivastava whose telephone number is (571) 272-0923. The examiner can normally be reached on Monday to Thursday from 7:30 A.M. to 6:00 P.M. (Eastern Standard or Daylight Savings Time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Jon Weber can be reached at (571)-272-0925 Monday through Thursday 7:30 A.M. to 6:00 P.M. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding may be obtained from the Patent Application Information Retrieval (i.e., PAIR) system. Status information for the published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (i.e., EBC) at: (866)-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Dr. Kailash C Srivastava/
Examiner, Art Unit 1657

Kailash C. Srivastava, Ph.D.
Patent Examiner
Art Unit 1657
(571) 272-0923

02 August 2008
/David M. Naff/
Primary Examiner, Art Unit 1657